Melanotic Tumors in *Drosophila*.*

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At least 24 different strains of *Drosophila* which develop tumors have been described (1). A few, such as *me*, probably represent the end result of a degenerative rather than a neoplastic change (4). All except one of the remainder have tumors which are melanotic. They are usually present in only a portion of the animals, although those without tumors transmit the susceptibility to their progeny. In the 8 stocks we have studied the incidence ranges from less than 1% to 50%. The tumors appear early in larval life and become pigmented. With metamorphosis the cellular elements regress, leaving a residue of pigment by which they are identified grossly. The tumors which we have observed are benign, their characteristic size and location varies from one strain to another, and multiple tumors are not uncommon. They also survive transplantation.

Sections reveal that the tumors are composed of polyhedral cells in clusters and fusiform cells may also be present. The tissue of origin has been inferred from the location and superficial resemblance to adjacent structures, but such conclusions are open to question (6). In the adult, amorphous pigment is all that remains.

These stocks of *Drosophila* have been inbred and isogenic strains isolated. It is possible not only to find the chromosomes responsible for tumor susceptibility in *Drosophila* but also to determine the locations of the genes involved on a specific part of each chromosome in certain instances. The number, location, and action of genes varies among the strains. Also certain tumor genes from one strain may affect tumor susceptibility when introduced into another tumor stock. Genes affecting tumor susceptibility have been found on the X chromosome and the three autosomes. Some modifying genes may enhance susceptibility while others suppress it. A single gene near the left end of the X chromosome is responsible for the *lethal 7* tumor (2). On the other hand, Stark reports that there are genes on four chromosomes affecting tumor incidence in *be-3* (5). The second chromosome is largely responsible for the presence of tumors in tu^{9} and tu^{48j}.

The incidence of these melanotic tumors is affected by the environment in which the flies are raised. There are usually fewer tumors when cultures are crowded, and nutrition, temperature, and irradiation also influence the number of tumors which appear. Therefore it is very important to maintain uniform culture conditions when studying the tumors.

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We have also used *Drosophila* to investigate chemical mutagens and carcinogens. Reports of the parallelism between carcinogenic and mutagenic properties of certain chemicals has lent support to the hypothesis that mutations play an important role in the etiology of tumors (3). In our laboratory results to date indicate that carcinogens are not always mutagens although they may be in some instances. Methyl-*bis* (betachloroethyl) amine hydrochloride and 20-methylcholanthrene have been administered to flies and tests made for lethal mutations on the X chromosome. Using nitrogen mustard, 149 mutations were found in 17,052 chromosomes tested. Eight parents were responsible for 67 of these lethals which were probably carried over from a previous generation since the material was administered serially. Methylcholanthrene was administered as a vaginal douche and also as an aerosol. There were 3 mutations in 4.660 chromosomes tested in the former and 10 in 10,108 in the latter. Untreated flies showed 2 mutations among 2.822 chromosomes tested. In contrast to the data for nitrogen mustard, these results do not support the idea that methylcholanthrene is a mutagen, although the low mutation rate might be due to strain or species differences in response or to insufficient dosage for the mode of administration.

The use of *Drosophila* as a test animal in the study of atypical growth thus presents certain advantages. This is particularly true for the study of hereditary factors which are active in many and diverse types of neoplastic disease. Both hereditary and environmental factors are relatively easily controlled, the chromosome number is small, the life cycle is short, and the mutation rate may be determined in an objective manner. Experiments with tumors in *Drosophila* may have added significance because of certain similarities to mammalian atypical growth. In this animal we already have concise evidence of gene action in tumor formation, and further study may be equally informative.

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